

**REMARKS/ARGUMENTS**

Claims 23, 24, 26 and 28-37 have been examined. Applicant's submission filed on August 15, 2007 has been entered and the request for continued examination has been accepted removing the finality of the previous Office Action. Applicants respectfully request reconsideration of the application light of the above amendments and the following remarks.

Rejections Under 35 U.S.C. §103

Claims 23, 31-32, 33-37 remain rejected under 35 USC §103(a) as being obvious over Sallusto *et al.*, (*J. Exp. Med.* 179:1109-1118, 1994), in view of Bigotti *et al.*, (*Prostate* 19:73-87, 1991), as evidenced by Inaba *et al.*, (*J. Exp. Med.* 166:182-194, 1987) for the reasons of record in the paper of February 15, 2007. Briefly, the reasons provided in that rejection included a summary of Sallusto *et al.* as teaching that exposure to GM-CSF plus IL-4 converts blood mononuclear cells to immature dendritic cells, that maintain the antigen capturing and processing capacity characteristics of immature dendritic cells *in vivo* and efficiently present soluble antigen, such as tetanus toxoid to specific T cell clones (abstract). Sallusto *et al.* is also asserted as teaching that dendritic cells (DCs) exist in two stages of maturation and teaching that as immature dendritic cells, they are capable of antigen capture/processing and immunostimulation, but as the dendritic cells mature, they lose antigen-capturing capacity. Sallusto *et al.* is further asserted as teaching that Langerhans cells represent immature dendritic cells in skin. Sallusto *et al.* also is believed by the Examiner to teach that the dendritic cells are from human peripheral blood. The Examiner admits that Sallusto *et al.* does not teach that the antigen is a prostate antigen or that the activation of T cells specific for prostate antigen is 2 to 3 fold more than that of the control.

Bigotti *et al.* is cited by the Examiner as teaching that Langerhans cells (LCs) are a type of dendritic cells capable of direct prostate antigen presentation to immune cells. The LCs are also asserted to be able to elicit the immune response and for providing a means for controlling the escape of cancer cells from the immune surveillance. Bigotti *et al.* is also said by

the Examiner to teach that Langerhans cells are found mainly in low grade prostate cancer, as opposed to the higher grades, and that the LCs represent a good prognostic indicator. Bigotti *et al.* is also asserted to teach that the number of Langerhans cells is directly correlated with the expression of HLA class II-DR molecules of tumor cells, and that Langerhans cells and HLA class II molecules provide a means of eliciting the immune response. Further, the Examiner alleges that Bigotti *et al.* teach that it is commonly believed that the antigen presenting properties are dependent upon HLA class II expression.

Based on the above summary of the cited references the Examiner has concluded that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to obtain human, immature dendritic cells, using the method taught by Sallusto *et al.*, and to replace the antigen tetanus toxoid taught by Sallusto *et al.* with a prostate antigen taught by Bigotti *et al.*, for exposure of the prostate antigen to the immature dendritic cells, because the dendritic cells, such as Langerhans' cells, would present prostate antigen to immune cells, and activate specific immune response, and thus, would provide treatment of prostate cancer.

Moreover, the Examiner has asserted that one would have a reasonable expectation of success, because the immature dendritic cells, obtained from culture in GM-CSF and interleukin-4, maintain the antigen capturing and processing capacity characteristics of immature dendritic cells *in vivo*, and efficiently present soluble antigen, as taught by Sallusto *et al.*, and the Examiner has further alleged that because Langerhans cells, which are a type of dendritic cell, are found mainly in low grade prostate cancer, as opposed to the higher grades, and represent a good prognostic indicator, and further because the Langerhans cells are capable of direct prostate antigen presentation to immune cells, and eliciting the immune response, as taught by Bigotti *et al.*

In addition, the Examiner has alleged that it would have been obvious to obtain blood mononuclear cells from a prostate cancer patient for converting to immature dendritic cells, because the dendritic cells from the prostate cancer patient would be readily available, and

would not require donor blood mononuclear cells, and because one would have expected that blood mononuclear cells from a prostate cancer patient would also be able to be converted to immature dendritic cells, using the method taught by Sallusto *et al.*

Still further, the Examiner has asserted it would have been obvious to match the dendritic cells isolated from a normal individual with HLA of the recipient, because dendritic cells, such as Langerhans cells, are directly correlated with HLA class, as taught by Bigotti *et al.*, and thus would not present the antigen with non-matched HLA cells.

The Examiner has conceded that the references do not explicitly teach that the dendritic cells can activate 2 to 3 fold more T cells specific to the prostate antigen as compared to a cell population cultured in the presence of granulocyte- macrophage colony-stimulating factor, interleukin-4, that has not been exposed *in vitro* to the prostate antigen, however, the Examiner has alleged that the immature dendritic cells taught by Sallusto *et al.*, after exposure to a prostate antigen, would present the prostate antigen, and be able to activate 2 to 3 fold more T cells specific to the prostate antigen, because the immature dendritic cells taught by Sallusto *et al.* are produced by the same process as disclosed in the specification of the instant invention, i.e. cultured in the presence of GM-CSF and IL-4. The Examiner believes the claimed dendritic cells to be the same as the dendritic cells taught by the combined art, absent a showing of unobvious differences. Further, the Examiner has stated that as the office does not have the faculties and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product in the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences.

Applicants prior arguments have been considered by the Examiner and found to be unpersuasive. In particular, the Examiner has asserted that the motivation for replacing the model antigen tetanus toxin in the method taught by Sallusto *et al.* with the prostate antigen taught by Bigotti *et al.* is to make *in vitro* dendritic cells that have the ability to present the

prostate cancer antigen using the method taught by Sallusto *et al.* for potential use in treating prostate cancer in view that the presence of dendritic cells, *eg.*, Langerhan's cells, is correlated with low grade prostate cancer. Further, the Examiner has asserted that further motivation is found in the presence of Langerhan's cells in prostate cancer is a good prognostic indicator as taught by Bigotti *et al.*

Applicants must again strongly disagree with the Examiner's combination of the cited references. In particular, the Examiner has concluded that the references can be properly combined and that in combining the teaching of Sallusto *et al.* and Bigotti *et al.* it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to obtain human, immature dendritic cells, using the method taught by Sallusto *et al.*, and to replace the antigen tetanus toxoid taught by Sallusto *et al.* with a prostate antigen taught by Bigotti *et al.*, for exposure of the prostate antigen to the immature dendritic cells, because the dendritic cells, such as Langerhans' cells, would present prostate antigen to immune cells, and activate specific immune response, and thus, would provide treatment of prostate cancer.

Bigotti *et al.* do not teach a prostate antigen for any purpose. The Examiner has cited to the abstract and to page 85 of Bigotti *et al.* as supporting the conclusion that a prostate antigen is taught to replace the tetanus toxoid of Sallusto *et al.*. As noted in the prior response there is no teaching of a prostate antigen found in either the abstract or on page 85 of Bigotti *et al.* or anywhere else in the article. The statement in the abstract that comes closest to the Examiner's contention reads: "... , since LCs and HLA class II molecules may provide a means of eliciting the immune response, both LCs and epithelial cells expressing class II molecules being capable of direct antigen presentation to immune cells." The Examiner infers that Bigotti *et al.* teach presentation of *prostate antigen* to the immune system. Applicants respectfully submit that this interpretation of the language in Bigotti *et al.* is not correct and that the Examiner is using Applicants' disclosure to reconstruct the present invention. The teachings of Bigotti *et al.* cited by the Examiner, such as the correlation of LC and tumor grade, the expression of class II molecules by LCs and tumor cells, and the dependence of antigen presenting properties on class II expression, have no bearing on the pending claims, since these

characteristics when either considered alone or in any combination, do not infer that human DC exposed *in vitro* to a prostate antigen can uptake and present the prostate antigen and activate T cells specific to the prostate antigen, which is the subject matter of the present claims.

In fact, a careful reading of Bigotti *et al.* by one skilled in the art would lead to different conclusions than those set forth by the Examiner. In particular, if in fact the LCs present in the low grade carcinomas were to present prostate antigen to the immune system, one skilled in the art would expect infiltration of immune cells to those locations. Indeed, Bigotti *et al.* examine their histological samples for such infiltrates. (See page 77 bridging to pages 78 and 79). Bigotti *et al.* state "[f]inally we examined all the sections for lymphoid infiltrate, but we found that lymphocytes were scarce in all the tumors, regardless of the degree of differentiation, and were mostly present at the peripheral border of the tumor as small aggregates." "Instead we found that low-grade carcinomas were very rich in HLA class II-positive, interstitial, oval to elongated cells, which were sometimes in close contact with tumor glands (Fig 12), mostly representing macrophages and in only small percentages LCs, as comparing the adjacent S-100-stained section." These results are reviewed in the discussion section found on pages 82-85 of Bigotti *et al.*, where the authors state "[l]astly, we did not find a correlation among cytological grade, HLA-class II expression, LCs, and lymphoid infiltrate as the latter was present mostly at the periphery of tumors as aggregates and did not show close contact with the malignant glands; instead we found a correlation among the aforementioned parameters and the presence of interstitial oval to elongated HLA class II positive cells, interpretable as macrophages, histiocytes, and activated fibroblasts; comparison with the corresponding S-100-stained section showed only a minimal part of these cells corresponded to LCs." The authors' final conclusion was that as there was evidence in the art to support that macrophage play an important roll in tumor rejection, the environment described by their results indicated that a similar mechanism was involved. Clearly, Bigotti *et al.* correlate tumor rejection and lymphocytic infiltrates with the presence of macrophage and not with the presence of LCs. Therefore, the reference would direct the skilled artisan away from combining the references as suggested by the Examiner and

towards the use of macrophage to induce immune-mediated tumor rejection. In the present Office Action the Examiner has not provided any reasoning or teachings that address this issue.

Further, the Examiner addresses Applicants remarks concerning immunosuppression by secreted IL-10 by cancer cells taught by prior art references submitted with Applicants prior response. In particular, the Examiner has concluded that immunosuppression does not apply to the low grade prostate cancer environment taught by Bigotti *et al.* because Steinbrink *et al.* allegedly "teach a correlation between advanced cancers, such as those having metastasis, and the elevated level of IL-10, which elevated level of IL-10 suppresses the immune response by T cells, by inducing anergy of T cells." Further, the Examiner asserts that none of the references cited by Applicants in the prior response teach the suppression of T cell response by IL-10 in prostate cancer. Steinbrink *et al.* is also alleged by the Examiner to teach that depending on the type of tumor, IL-10 actually has the reverse effect, for example, stimulating immunogenicity and rejection of the tumor.

Applicants must disagree with the Examiner's characterization of the prior remarks regarding Bigotti *et al.* and to the Examiner's characterization of Steinbrink *et al.* In particular, as previously noted, Bigotti *et al.* provides no information control group to compare the number of LCs in the low grade tumor samples with normal prostate tissue. The Examiner has not addressed this issue. To further support this point Applicants provide herewith a copy of an abstract of Troy *et al.*, *J. Urol.* 160:214-219, 1998, wherein the number of Langerhans cells and the number of dendritic cells were compared between prostatic cancer tissue and adjacent normal prostate tissue. The authors state that the number of dendritic cells and Langerhans cells in the normal tissue were greater than in the normal prostatic tissue. They conclude that "there is no active recruitment of DC into prostate cancer and those DC present are only minimally activate. Further, Applicants provide herewith a copy of Sharma *et al.*, *Cancer Res.* 59:2271-2276, 1999 which provides that Dunning R-3327 rat prostatic adenocarcinomas cells, a widely accepted model for *in vivo* experimental studies of prostate cancer, when implanted into rats secrete IL-10. Sub-clones of the R-3327 cells that were selected for differential properties of tumor formation and metastasis. Both the metastatic sub-clone and the epithelial-like sub-clone were found to

secrete IL-10. As such, Applicants believe that Bigotti *et al.* does not suggest to one of skill in the art that any LCs found in a low grade prostate tumor must be present to uptake and present prostate antigen to T cells as suggested by the Examiner. Bigotti *et al.* merely suggest that the present of LCs can be used to classify prostate tumor.

As to the passages in Steinbrink *et al.* regarding the possible reverse effects of IL-10 in some tumors, Applicants direct the Examiner to, in particular, paragraph 3, right column, page 1640 where the authors report "[t]hese contrasting results might be due to the different tumor models use, the varying amounts of IL-10 used, and the different forms of IL-10 (virus IL-10 v IL-10) applied. It was demonstrated that the antitumor effect of IL-10 was dose-dependent and that only very high levels of IL-10 were effective in tumor rejection." The authors continue to conclude that in their model, pretreatment of human DC with IL-10 induces a state of antigen-specific anergy in cytotoxic CD8<sup>+</sup> T cells. Applicants believe that Steinbrink *et al.* supports the conclusion that IL-10 is an immunosuppressive agent normally found in many tumors. The additional references cited herein demonstrate that prostate tumor secrete IL-10 and that Bigotti *et al.* would be interpreted as merely demonstrating a means for classifying prostate tumor samples.

The Examiner further declares in response to "Applicants assertion" that Bigotti *et al.* refer to membrane bound prostate cancer antigens, and not soluble antigen is required by the instant claims that it is well known in the art that cancer cells shed their cancer antigens in the vicinity of cancer cells and that exposure to soluble antigen to immature dendritic cells *in vitro* in the present of GM-CSF and IL-4 to induce maturation, and their ability to present soluble antigen is taught by Sallusto *et al.*

Applicants again must disagree with the Examiner. Applicants note that the remarks relating the soluble antigen where in regard to the response to the citation by the Examiner of a quote from Bigotti *et al.* Applicants noted that the quote refers to membrane bound tumor associate antigens, not soluble antigen as required by the claims of the present invention. The Examiner is now alleging that it is well known to the skilled artisan that tumors

generally are known to secrete tumor antigen and that one would have expected soluble antigen in the vicinity of cancer cells. As above, the Examiner has not addressed the issue of the presence of an immunosuppressive environment in the tumor. As above, prostate cancer cells, as exemplified by the rat R-2377 cells, secrete IL-10. Further, prostate tumors were well known to be weakly immunogenic, and as above, the number of dendritic cells and Langerhans cells were known to be less in prostatic tumor than in adjacent normal prostatic tissue. As such, the presence of any soluble tumor antigen in the tissue of Bigotti *et al.* is irrelevant to the rejection made by the Examiner.

The Examiner in addition, that the information Applicants included regarding B7 argues a limitation not in the claims. Applicants must disagree, in that the information regarding B7 was only included to the quote cited by the Examiner in Bigotti *et al.* teaching soluble prostate antigen. In that, the information provided by Bigotti *et al.* is insufficient in of itself to reach the conclusion alleged by the Examiner. To reach the conclusion, Applicants argued that without additional information relating to, for example, the expression of B7-1 (CD80) and B7-2 (CD86), it is just as likely that the Langerhans cells are involved in a tumor escape mechanism. Whether the Langerhans cells present in the samples of Bigotti *et al.* would depend on the state of maturation of the cells which in turn is dependent on the tumor milieu. As the Examiner has not made a case regarding the extrapolated teachings of Bigotti *et al.* no conclusions can be reached regarding to state of reason for the presence of the Langerhans cells in the prostate sample and no reason is provided to combine Bigotti *et al.* with Sallusto *et al.* to obtain the invention encompassed by the claims of the present invention.

Claim 24 remains rejected under 35 USC §103(a) as being obvious over Sallusto *et al.*, in view of Bigotti *et al.*, as evidenced by Inaba *et al.*, *supra*, and further in view of Cohen *et al.*, (*Cancer Res.* 54:1055-1058, 1994) for the reasons of record. Briefly, the teachings of Sallusto *et al.*, Bigotti *et al.*, and Inaba *et al.* have been set forth above. Further, the Examiner has acknowledged that Sallusto *et al.*, Bigotti *et al.*, and Inaba *et al.* do not teach that the antigen is a lysate of prostate tumor cells. The Examiner believes that Cohen *et al.* teach that syngenic dendritic cells, when pulsed with tumor lysate, induce antigen-specific proliferation of antitumor



CD4<sup>+</sup> T cells, relevant to the rejection of the syngenic methylcholanthrene tumor (abstract) and that it would have been obvious to use as prostate antigen, a lysate of prostate cancer cells from a prostate cancer patient, because prostate cancer cells would have several prostate cancer-specific antigens. The Examiner also believes that it would have been obvious to use a tumor lysate because Cohen *et al.* teach that a tumor lysate successfully primes the dendritic cells for inducing antigen-specific proliferation of antitumor CD4<sup>+</sup> T cells and the Examiner believes that it would be more convenient to use tumor lysate because it does not require the extra step of purification of the antigen.

The Examiner has consider Applicants prior response and has found it to be unpersuasive. In particular, the Examiner believes that the combination of Sallusto *et al.* and Bigotti *et al.* suggests the compositions of the claims invention as set forth above. Further, the Examiner alleges that it would have been obvious to use as prostate antigen a lysate of prostate cancer cells from a prostate cancer patient for the other reasons of record as recited above.

As above, the combination of Sallusto *et al.* and Bigotti *et al.* fail to teach the compositions of the present invention. Instead, Bigotti *et al.* teach that macrophage likely induce the immune response seen in prostate cancer and that the presence of Langerhans cells can be used to stage prostate cancer tissue. As such, any combination with Inaba *et al.* and/or Cohen *et al.* can not provide the skilled artisan with incentive to combine the references to use a lysate of prostate cancer cells from a prostate cancer patient to make the compositions of the claim 24.

Claim 26 remains rejected under 35 USC §103(a) as being obvious over Sallusto *et al.*, in view of Bigotti *et al.*, and as evidenced by Inaba *et al.*, *supra*, as applied to claim 23, and further in view of Lutz *et al.* for the reasons already of record. Briefly, the reasons are that the teaching of Sallusto *et al.*, Bigotti *et al.*, and Inaba *et al.* as summarized by the Examiner has been set forth above and that although the Examiner has concluded that Sallusto *et al.*, Bigotti *et al.* and Inaba *et al.* do not teach dendritic cells that are extended life span dendritic cells, the Examiner believes that Lutz *et al.* teach making immortalized dendritic cells (Abstract), which overcomes the problem of being unable to maintain dendritic cells *in vitro* for long periods of

time (p. 278). Therefore, the Examiner believes that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to immortalize the dendritic cells taught by Sallusto *et al.*, Bigotti *et al.*, and Inaba *et al.*, using the immortalizing method taught by Lutz *et al.*, because immortalizing dendritic cells would enable maintenance of dendritic cells *in vitro* for long periods of time, as taught by Lutz *et al.*

The Examiner has considered Applicants prior response and it has not been found to be persuasive. In particular, as above, the Examiner believes that the combination of Sallusto *et al.*, Bigotti *et al.* and Inaba *et al.* suggests the compositions of the present invention as set forth above. It is alleged by the Examiner that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to immortalize the dendritic cells taught by the combination of the cited references and to use the methods of Lutz for the reasons above.

As above, the Sallusto *et al.*, Bigotti *et al.* and/or Inaba *et al.* when considered either alone or in combination do not teach the compositions of the present invention. As such, the addition of Lutz *et al.* allegedly teaching immortalization of dendritic cells can not provide the skilled artisan with motivation to make the composition as set forth in claim 26.

Claims 28-29 remain rejected under 35 USC §103 as being obvious over Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.*, and Cohen *et al.*, *supra*, as applied to claim 23, and further in view of Taylor *et al.* for the reasons of record in Applicants' prior response. Briefly, the teachings of Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.* and Cohen *et al.* as set forth by the Examiner has been set forth above. In addition, although the Examiner acknowledges that Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.*, and Cohen *et al.* do not teach that the dendritic cells are cryopreserved, the Examiner believes that Taylor *et al.* teach cryopreservation of dendritic cells, wherein said cryopreserved dendritic cells can be used in immunological procedures. As such, the Examiner believes that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to cryopreserve the dendritic cells taught by Sallusto *et al.*, Bigotti *et al.*, Stites (was Inaba *et al.* intended?), and Cohen *et al.*, using the

cryopreservation method taught by Taylor *et al.*, to preserve the previously isolated dendritic cells for later use.

The Examiner has considered the response as set forth by Applicants and found that the arguments are not persuasive. In particular, the Examiner alleges that the combination of Sallusto *et al.*, Bigotti *et al.* and Inaba *et al.* suggests the composition of the claimed invention as set forth above. Further, the Examiner has alleged that it would have been *prima facie* obvious for the reasons set forth above from the prior office action.

Applicants must again disagree with the reasoning of the Examiner. In particular, as above, Sallusto *et al.*, Bigotti *et al.* and Inaba *et al.*, do not teach the compositions of the present invention. Taylor *et al.* is directed to cryopreservation techniques and does not address the teachings of Bigotti *et al.* Bigotti *et al.* teaches that the immune response is likely induced in prostate cancer by macrophage. As such, Sallusto *et al.*, Bigotti *et al.* and Inaba *et al.*, when considered individually or in any combination does not teach or suggest the composition as set forth in claims 28 and 29.

Claim 30 remains rejected under 35 USC §103 as being obvious over Sallusto *et al.*, Bigotti *et al.*, and Inaba *et al.*, *supra*, as applied to claim 23, and further in view of Taylor *et al.* as applied to claim 28, and Lutz *et al.*, for the reasons of record. Briefly, the teachings of Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.* and Taylor *et al.* as set forth by the Examiner have been set forth above. The Examiner has noted that Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.* and Taylor *et al.* do not teach that the dendritic cells have extended life, but the Examiner believes that Lutz *et al.* teach making immortalized dendritic cells, which overcomes the problem of being unable to maintain dendritic cells *in vitro* for long periods of time. As such, the Examiner believes that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to immortalize the cryopreserved dendritic cells taught by Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.* and Taylor *et al.*, using the immortalizing method taught by Lutz *et al.*, because immortalizing dendritic cells would allow maintenance of dendritic cells *in vitro* for long periods of time, as taught by Lutz *et al.*

The Examiner has considered the arguments set forth in Applicants' response, by has not found them to be persuasive. In particular, the Examiner believes that the combination of Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.* and Taylor *et al.* suggests the composition of the claimed invention and that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to immortalize the cryopreserved dendritic cells for the reasons set forth above.

Applicants must again disagree with the rejection of the Examiner, as above, the teachings of Sallusto *et al.*, Bigotti *et al.*, Inaba *et al.* and Taylor *et al.* do not disclose or suggest the compositions of the present application. The teachings of Lutz *et al.* when considered either alone or in combination with any of the other cited references does not cure the deficiencies of the primary references, Sallusto *et al.* and Bigotti *et al.* in that Bigotti *et al.* teaches away from the compositions of the present invention.

In view of the above remarks, Applicants respectfully request the Examiner to reconsider and withdraw the various rejections of claims 23, 24, 26, and 28-37 under 35 U.S.C. § 103(a) as being obvious over Sallusto *et al.*, Bigotti *et al.* as evidenced by Inaba *et al.*, in view of Stites, and Cohen *et al.*, alone and in various combinations. In particular, Bigotti *et al.* teaches away from the compositions of the present invention by teaching that the immune response to prostate cancer is likely induced by macrophage and that Bigotti *et al.* teach no more than a method for staging prostate tumor samples. In light of the teachings of Bigotti *et al.* the skilled artisan would not have been motivated to produce the compositions of the present invention.

Appl. No. 09/016,737  
Amdt. dated April 16, 2008  
Reply to Office Action of October 16, 2007

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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